Xia, alone or in view of the other cited references, does not render the present claims unpatentable.

The claims, in one aspect of the present invention, are directed to antibodies which bind to the same epitope on human lymphocytes as the antibody produced by the deposited cell line.

In another aspect of the present invention, as defined broadly in Claim 38, the present invention is directed to a composition which comprises an antibody which binds to the same epitope on human lymphocytes as the antibody produced by the deposited cell line, and a pharmaceutically acceptable carrier. The antibody is present in the composition in an amount effective to inhibit a T-cell mediated immune response.

During prosecution of parent application Serial No. 08/472,281, the Examiner acknowledged that the antibody produced by such cell line is patentable over the prior art.

The issue remains whether or not one skilled in the art from reading Xia, et al. would be enabled to obtain an antibody which binds to the same epitope as the antibody produced by the deposited cell line.

In support of Applicants' position, Applicants submit herewith a copy of a Declaration by Dr. Barbara E. Bierer, which was filed in parent application Serial No. 08/472,281.

Applicants assert that if, as the Examiner recognized during prosecution of parent application Serial No. 08/472,281, one skilled in the art could not produce the deposited antibody, one skilled in the art also would not be enabled by Xia to produce an antibody which binds to the same epitope.

As indicated in the Declaration of Dr. Bierer, the characteristics which are defined in Xia, et al. are not characteristics which define a specific epitope. The characteristics disclosed by Xia are characteristics common to CD2 antibodies as a class. Thus, even if one skilled in the art were able to identify an antibody which had characteristics similar to those of the LO-CD2a antibody disclosed in Xia, et al., such characteristics do not indicate whether or not an antibody binds to the same epitope as the deposited antibody in that such characteristics are those generally possessed by CD2 antibodies.

As indicated in Dr. Bierer's declaration, from the teachings of Xia, one skilled in the art would have no way of knowing which, if any, of the antibodies which would be produced by the general procedure disclosed by Xia, et al. is LO-CD2a or which binds to the same epitope as the antibody of the present invention in that the characteristics disclosed by Xia do not define LO-CD2a uniquely (distinguishing LO-CD2a from CD2 antibodies as a class) or define which antibodies bind to the same epitope as LO-CD2a or deposited antibody.

The claims of the present application are directed to an antibody which binds to the same epitope as the antibody produced by the deposited cell line. In order to negate the patentability of such claims, it is incumbent upon the Examiner to provide detailed reasons as to why he believes that the characteristics disclosed by Xia uniquely define antibodies which bind to the same epitope as the antibody produced by the deposited cell line, particularly in view of the Declaration of Dr. Bierer, which indicates clearly that the characteristics included in Xia, et al. are characteristics which are known to be present in CD2 antibodies as a class, and do not define whether or not an antibody binds to a particular epitope. In particular, as noted by Dr. Bierer, different antibodies which bind to

different epitopes have the characteristics disclosed by Xia and, therefore, such characteristics are not suitable for identifying an antibody as claimed.

In view of the fact that Xia does not disclose or render obvious to one of ordinary skill in the art the antibody produced by the deposited cell line and further in view of the fact that the characteristics disclosed by Xia are not characteristics which are related to a specific epitope, Xia does not disclose or render obvious to one of ordinary skill in the art an antibody which binds to the same epitope as the antibody produced by the deposited cell line.

Although Xia at Page 320 indicates that the LO-CD2a antibody binds to an epitope which is different from other antibodies referred to on Page 320, Xia does not identify the epitope to which LO-CD2a binds. Because Xia does not define the epitope, Xia does not make LO-CD2a available to one skilled in the art, and one skilled in the art would not have sufficient information to determine whether or not a produced antibody bound to the same epitope as LO-CD2a. The information provided on Page 320 at best permits one skilled in the art to determine that a produced antibody is not D66. Such information does not enable one to determine whether a produced antibody is LO-CD2a, or an antibody other than LO-CD2a.

In addition, the prior art does not provide any reasonable expectation that the claimed antibody or a composition including such antibody in combination with a pharmaceutically acceptable carrier could be used successfully in a human. In fact, the prior art as a whole suggests that CD2 antibodies would not be successful.

In this respect, Thurlow et al. (Transplantation, Vol. 36, pages 293-97), copy attached, reports that an attempt to use a CD2 monoclonal antibody in a human was not successful.

Giorgi (Transplantation Proceedings, Vol. 15) reports that another CD2 antibody was not successful in primate studies.

Thus, there is nothing in the prior art which would lead one to expect that the claimed compound could be used in treating patients.

The Examiner's attention is drawn to Pages 40-43 of the Specification which provides human data. It is noted that the human data shows successful treatment after onset of rejection; *i.e.*, the treatment can reverse rejection.

This should be contrasted with the indication in the prior art that CD2 antibodies if effective at all would be effective only if administered immediately after T-cell priming (Guckel, Page 964, Paragraph bridging Col. 1 and 2).

As the Examiner is no doubt aware, in treating rejection or other T-cell mediated responses, it is virtually impossible to treat within 24 hours of antigen "priming."

Thus, the ability to treat patients successfully in accordance with the invention would not be expected from the prior art. In fact, the prior art suggests that CD2 antibodies would not be suitable for the treatment of patients.

The claimed subject matter is directed to an antibody which binds to the same epitope as the antibody produced by the deposited cell line. The totality of the evidence, including the Declaration of Dr. Bierer, indicates that the characteristics disclosed by Xia, et al. are <u>not</u> sufficient to identify LO-CD2a in a manner which distinguishes LO-CD2a

from CD2 antibodies as a class or to enable one skilled in the art to identify antibodies which bind to the same epitope as the antibody produced by the deposited cell line.

In addition, Applicants have found unexpectedly that the claimed antibody may be employed to treat humans, contrary to the accepted wisdom of the prior art. Such findings, therefore, are a clear indication of the nonobviousness of the claimed antibody as employed in combination with an acceptable pharmaceutical carrier for treating humans. (See W.L. Gore and Associates, Inc. v. Garlock Inc., 220 U.S.P.Q. 303 (C.A.F.C. 1983), at 312; United States v. Adams, 383 U.S. 39 (1966)).

Also, because the prior art does not disclose or even remotely suggest to one of ordinary skill in the art that the claimed antibody may be used to treat humans, the cited prior art does not render obvious to one of ordinary skill in the art the combination of the claimed antibody and an acceptable pharmaceutical carrier, as defined in Claim 38, even if, assuming solely for the sake of argument, the claimed antibody were known. (See Ex Parte Erdmann, 194 U.S.P.Q. 96 (Bd. App. 1976), at 97.) The prior art, therefore, provides no basis for the claimed invention, and does not render the claimed invention obvious to one of ordinary skill in the art within the meaning of 35 U.S.C. 103.

With respect to the rejection of Claims 34 and 42, under 35 U.S.C. 112, second paragraph, although the term "chimeric" may include a variety of antibodies, such term is well known to those skilled in the art, and therefore such term does not render the claims indefinite. One skilled in the art could determine readily whether a particular antibody is a chimeric antibody and whether such an antibody binds to the same epitope on human lymphocytes as the antibody produced by the deposited cell line, and thus infringe Claims 34 and/or 42. For the above reasons and others, Claims 34 and 42 are not indefinite, and it

is therefore respectfully requested that the rejection under 35 U.S.C. 112, second paragraph, be reconsidered and withdrawn.

For the above reasons and others, this application is in condition for allowance, and it is respectfully requested that the rejections be reconsidered and withdrawn and a favorable action is hereby solicited.

Respectfully submitted,

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